REMARKS

Favorable reconsideration is respectfully requested in view of the added claims and the following comments.

By this Amendment, new claims 35-43 have been added. Claims 21-43 are pending in the application.

The newly presented claims find clear antecedent support in the second, third, sixth and final paragraphs on page 2 of the specification, the second and third paragraphs on page 3 of the specification, the text from the third paragraph on page 3 to the second paragraph on page 4 of the specification, and the second and third paragraphs on page 7 of the specification.

In view of the fact that the number of claims now exceed 20 by three additional claims, a remittance in the amount of $54.00 accompanies herewith.

The rejection of claims 21-34 "under 35 U.S.C. 103(a) as being unpatentable of U.S. Patent 5,260,069 to Chen in view of WO 97/02020 to Dietrich *et al.*" is respectfully traversed. This ground of rejection is based on a combination of references, current criteria for which are set forth, e.g., in the opinion for *In re Lee*, 61 U.S.P.Q.2d 1430 (Fed. Cir. 2002), at 1433 and 1434:

> "The factual inquiry whether to combine references must be thorough and searching." It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with. "[P]articular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed." The Examiner can satisfy the burden of showing obviousness of the combination "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." The Board rejected the need for any specific hint or suggestion in a particular reference" to support the combination of the two

references. Omission of a relevant factor required by precedent is both legal error and arbitrary agency action.

As outlined under "prior art" on pages 1 and 2 of the specification, conventional oral administration forms for pyridin-2-ylmethylsulfinyl-1H-benzimidazoles are designed to have an outer enteric coating to protect the core with the active ingredient from exposure of gastric acid. The present application is directed to the following finding:

> Surprisingly, it has now been found that an enteric coating for pyridin-2-ylmethylsulfinyl-1H-benzimidazoles is unnecessary if the coating used instead of it is designed so that the active compound is released only after a defined time, namely, after gastric passage. Furthermore, it has surprisingly been found that, with a suitable design of the core comprising the active compound, the release of the active compound - once it has commenced - takes place within a short space of time, so that a rapidly rising and high active compound blood level is achieved.
>
> The invention thus relates to an oral administration form for pyridin-2-ylmethylsulfinyl-1H-benzimidazoles and their salts, which comprises the active compound together with tablet disintegrants and is provided with a film coating, which is customary *per se* for sustained-release compositions.

Dietrich relates to a gastric acid protected (i.e., enteric coated) oral dosage form. As stated by the Examiner, the Dietrich reference teaches that the slow release form has a core, at least one intermediate layer controlling release of the active agent and an outer enteric layer, which is soluble in the small intestine. Enteric layers will not release the active compound during gastric passage but

only when coming into contact with the "basic" environment of the intestine. This means for the Dietrich reference formulations that release of the part of the pantoprazole, which is in slow-release form, can only be triggered after the tablet/pellet reaches the small intestine. From this it is clear that the slow release form of pantoprazole (which is "covered behind an enteric coating") according to the Dietrich reference will have a completely different release profile as compared to the administration form according to the invention, wherein the sustained release coating is not covered by an additional enteric coating.

The administration form having the coating film, which is customary *per se* for sustained release, does not have an enteric coating. By the combination of the tablet disintegrant and the sustained release coating according to the invention it has been found that the release of active compound - once it has commenced - takes place within a short space of time, so that a rapidly rising and high active compound blood level is achieved. It has been further found that the sustained release coating can be designed in a way to allow passage of the gastric tract and then immediately releasing the active compound in the small intestine. This now opens up the possibility to combine a tablet according to the invention with an enteric coating tablet.

With the aid of the oral administration form according to the invention, it is thus possible to simulate an administration of active compound at a later time. As a result, the possibility is opened up of allowing a once daily administration instead of a twice daily administration of the active compound to begin by combining, for example, in one and the same administration form (e.g., in a

capsule) two active compound forms whose release is different (e.g., a customary, enteric tablet and a tablet according to the invention).

Chen relates to a new dosage form, comprising a capsule containing pellets with varying rates of release. Chen does not address the problem of benzimidazoles, which are part of the present invention, which are sensitive to gastric acid. Neither Chen nor Dietrich suggest providing benzimidazoles without enteric coating, but with a sustained release coating (which surprisingly will completely and spontaneously release the active ingredient after gastric passage in the small intestine) and combining those with enteric coated tablets. Combining this novel administration form with enteric pellets will provide a beneficial effect for active compound blood levels and healing rate.

With the aid of the oral administration form according to the invention, it is thus possible to simulate an administration of active compound at a later time. As a result, the possibility is opened up of allowing a once daily administration instead of a twice daily administration of the active compound to begin by combining, for example, in one and the same administration form (e.g., in a capsule) two active compound forms whose release is different (e.g., a customary, enteric tablet and a tablet according to the invention).

In the fixed combination, both administration forms are present in a single dose unit (e.g., in a common tablet of outer conventional construction and inner core coated according to the invention, in a capsule comprising conventionally coated pellets and pellets according to the

invention or in particular in a capsule comprising two or more tablets, of which at least one corresponds to the specification according to the invention).

Independently of whether a fixed or free combination is present, the compliance in the case of the combination according to the invention is in any case considerably greater than when two conventional administration forms have to be taken in a relatively large space of time (for example in the space of 3 to 12 hours).

The two-fold administration of active compound simulated by the fixed or free combination leads in a relatively large space of time (compared with the same dose of active compound as a single administration) to a smaller width of variation in the active compound blood levels in the patients and moreover to more rapid symptom relief.

The Dietrich reference actually teaches away from using the Chen reference. In case the person skilled in the art would consider combining them, this could only result in using the Chen reference only with enteric coated tables. (On column 5, lines 26 to 31, Chen states that if required to resist dissolution in certain environments enteric coated tablets need to be used.)

The relevant art is defined as that "reasonably pertinent to the particular problem with which the inventor was involved." *Gargoyles Inc. v. U.S.*, 33 U.S.P.Q.2d 1595, 1600 (U.S. Ct. Fed. Cl. 1994). The problem the inventors (in their application) claim to have solved is relevant to the obvious inquiry. *Oscar Mayer Foods Corp. v. Con Agra Inc.*, 35 U.S.P.Q.2d 1278, 1281 (Fed. Cir. 1994). The crucial issue in defining the scope of relevant prior art is the "nature of the problem

confronting the would-be inventor." *Visual Security Concepts Inc. v. KTV Inc.*, 59 U.S.P.Q.2d 1268, 1271 (PA 2000).

When faced with the proposition of avoiding use of an enteric coating for protecting active ingredients of the type herein involved, nothing is found in the applied art that would leave any one of ordinary skill in the art to the selection of the particular art relied upon by the Examiner. Issue is respectfully taken with each and every allegation to the contrary, since no consideration is given therein to the state of the art regarding the involved pharmaceuticals.

Having overcome all outstanding grounds of rejection, favorable action on the merits is in order and is respectfully solicited.

Respectfully submitted,

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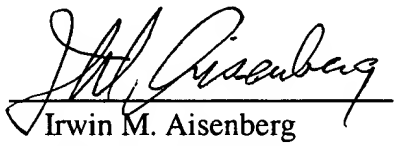
By: 
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Date: February 24, 2004
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